

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/00991

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 C07K14/71 A61K39/00 G01N33/53 C07K16/28		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07K A61K G01N		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) MEDLINE, BIOSIS, EPO-Internal, EMBASE, CHEM ABS Data, LIFESCIENCES, CANCERLIT, WPI Data, PAJ		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WOOD J M ET AL: "PTK787/ZK 222584, a novel and potent inhibitor of vascular endothelial growth factor receptor tyrosine kinases, impairs vascular endothelial growth factor-induced responses and tumor growth after oral administration." CANCER RESEARCH. UNITED STATES 15 APR 2000, vol. 60, no. 8, 15 April 2000 (2000-04-15), pages 2178-2189, XP000971163 ISSN: 0008-5472 abstract --- -/--	11
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "S" document member of the same patent family		
Date of the actual completion of the international search 14 August 2003		Date of mailing of the international search report 01/09/2003
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer Renggli-Zulliger, N

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>IGARASHI KATSUhide ET AL: "Tyrosine 1213 of Flt-1 is a major binding site of Nck and SHP-2."</p> <p>BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS,</p> <p>vol. 246, no. 1, 8 May 1998 (1998-05-08), pages 95-99, XP002251094</p> <p>ISSN: 0006-291X</p> <p>page 98, right-hand column, last paragraph</p> <p>-page 99; figures 2-4</p>	1-14
Y	<p>CARROLL RONA S ET AL: "KDR activation in astrocytic neoplasms."</p> <p>CANCER,</p> <p>vol. 86, no. 7,</p> <p>1 October 1999 (1999-10-01), pages 1335-1341, XP002251095</p> <p>ISSN: 0008-543X</p> <p>abstract</p>	1-14
Y	<p>TAKAHASHI T ET AL: "A single autophosphorylation site on KDR/Flk-1 is essential for VEGF-A-dependent activation of PLC-gamma and DNA synthesis in vascular endothelial cells."</p> <p>THE EMBO JOURNAL. ENGLAND 1 JUN 2001,</p> <p>vol. 20, no. 11, 1 June 2001 (2001-06-01), pages 2768-2778, XP002251096</p> <p>ISSN: 0261-4189</p> <p>cited in the application</p> <p>abstract; figure 1</p> <p>page 2769, left-hand column, paragraph 1</p>	1-14
A	<p>MENRAD A ET AL: "NOVEL ANTIBODIES DIRECTED AGAINST THE EXTRACELLULAR DOMAIN OF THE HUMAN VEGF-RECEPTOR TYPE II"</p> <p>HYBRIDOMA, LIEBERT, NEW YORK, NY, US,</p> <p>vol. 16, no. 5,</p> <p>1 October 1997 (1997-10-01), pages 465-471, XP002052460</p> <p>ISSN: 0272-457X</p> <p>abstract</p> <p>page 469</p>	1-14

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>ZHU Z ET AL: "Inhibition of vascular endothelial growth factor induced mitogenesis of human endothelial cells by a chimeric anti-kinase insert domain-containing receptor antibody." CANCER LETTERS. IRELAND 1 MAR 1999, vol. 136, no. 2, 1 March 1999 (1999-03-01), pages 203-213, XP002251097  ISSN: 0304-3835  abstract  page 210, left-hand column, last paragraph -right-hand column</p> <p>---</p>	1-14
A	<p>ROCKWELL P ET AL: "IN VITRO NEUTRALIZATION OF VASCULAR ENDOTHELIAL GROWTH FACTOR ACTIVATION OF FLK-1 BY A MONOCLONAL ANTIBODY" MOLECULAR AND CELLULAR DIFFERENTIATION, CRC PRESS, BOCA RATON, US, vol. 3, no. 1, 1995, pages 91-109, XP002052455  ISSN: 1065-3074  page 102, paragraphs 2,3  abstract</p> <p>---</p>	1-14
P,X	<p>MEYER ROSANA D ET AL: "The presence of a single tyrosine residue at the carboxyl domain of vascular endothelial growth factor receptor-2/FLK-1 regulates its autophosphorylation and activation of signaling molecules." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 277, no. 30, 22 May 2002 (2002-05-22), pages 27081-27087, XP002251098  July 28, 2002  ISSN: 0021-9258  abstract; figures 1,4-6</p> <p>-----</p>	1-14

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## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 9-11(partially)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 9-11(partially)

Present claims 9-11 relate to a product defined by reference to a desirable characteristic or property, namely comprising an inhibitor.

The claim covers all products having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products. In the present case, the claim so lacks support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search could not be carried out for the inhibitors disclosed in the present application since not a single example of such a substance is disclosed not even in example 2 where only inhibitors as a generic term are mentioned. The search has been restricted to antibodies and some chemical compounds (incomplete) that are inhibitors of the KDR/Flk-1 receptor.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.